Histamine Stimulation of Gastric Pepsin and Hydrochloric Acid in Patients of Vitiligo

SHUKLA and MUKERJI[1] observed that patients of vitiligo secreted subnormal amount of hydrochloric acid in the gastric juice. To find out how they responded to histamine stimulation, fractional gastric analysis was conducted in fifteen normal healthy individuals and thirty patients of vitiligo after subcutaneous injection of 0.01 mg of histamine acid phosphate/kg of body weight. Gastric secretions, aspirated every 5 min by syringe for 2 h, were later made into hourly volumes. In these hourly samples, free acid was found by titration against $N/10$ NaOH using phenolphthalein and Topfer's reagent as indicators, and pepsin was determined by GLICK's[2] modification of ANSON's[3] method using casein as the substrate. Hourly rate of output of free acid and pepsin was calculated from these volumes and concentrations.

The result was recorded in the Table.

The Table shows that both patients and normal subjects secrete 7–10 m.Eq. of hydrochloric acid/h. This amount of hydrochloric acid produces an approximate pH range of 2–3[4]. According to HOLLANDER[5], maximum conversion of pepsinogen to pepsin occurs at a pH range of 2–4.5. Therefore, at 2–3 pH, as observed in the experiment here, a maximum amount of pepsinogen would be changed to pepsin. Under these ideal conditions for formation of pepsin, it is found that patients of vitiligo are secreting two-thirds of the amount of pepsin to that secreted by the normal group.

The reduced value of enzyme in the stomach of patients will affect the hydrolysis of injested protein molecule at the more centrally located peptide linkage of α-carboxyl group of dicarboxylic amino acid and α-amino radical of aromatic amino acid[6]. The enzyme specifically splits this form of the peptide linkage which is present in L-tyrosine and L-phenylalanine residues[7]. Therefore, the deficiency of pepsin will interfere with the release of these amino acids. The action of the enzyme is quantitatively proportionate to the amount of pepsin[8], hence its lack will ultimately lead to a deficiency of amino acids phenylalanine and tyrosine. Phenylalanine is an essential amino acid[9] and along with tyrosine these form the basic substances for synthesis of melanine[10].

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Clinical category	No. of cases	Hourly output					
		Pepsin (Casein units)			HCl (m. Eq.)		
		Range	Mean	Median	Range	Mean	Median
Normal subjects	15	1920–51520	29039	34320	1.6–20	8.36	7.00
Vitiligo patients	30	1440–38400	21784	23020	0 –15	7.00	6.85

Therefore, it can be postulated that deranged synthesis of melanine in patients on vitiligo is induced by lack of secretion of pepsin. Detailed account of the work will be published elsewhere.

Zusammenfassung. Die stündliche Pepsinsekretion bei dreissig Vitiligo-kranken und 15 gesunden Personen wurde nach Histaminstimulation gemessen. Bei den Vitiligo-Kranken wurden zwei Drittel der normalen Pepsinsekretion beobachtet.

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The Influence of Reserpine upon the Changes in Femoral Blood Flow Produced by Stimulation of the Lumbar Sympathetic Chain[1]

The depletion of the norepinephrine stores in the heart[2–4] and in artery walls[5,6] is the likeliest explanation for the diminution of the characteristic response of the heart[7–9] and vessels to stimulation of adrenergic nerve fibers observed after pretreatment with reserpine. Recently graded doses of reserpine were found to cause a graded reduction in the effect of sympathetic nerve stimulation on myocardial contractility[9]. As an extension of these findings, the present study was designed to determine the relationship between reserpine dosage and function of the sympathetic nerves supplying the femoral vascular bed of the dog.

Under pentobarbital anesthesia and after 5 mg/kg heparin i.v. a double cannulation was made in the left external iliac artery of 18 dogs (7.1–14.8 kg). Blood from the proximal cannula was led through a Shipley-Wilson rotameter and back into the distal cannula. The perfusion pressure was measured from a sidearm placed just before the distal cannula. A sidearm placed just before the flowmeter was connected to the right external jugular vein so that, in order to lower the perfusion pressure, blood could be shunted away from the leg at will. The lungs were ventilated artificially with air. A thermometer was placed between the toes and the temperature was kept at

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33–35° C by means of an infrared lamp directed on the left thigh. The distal end of the left lumbar sympathetic chain, cut at L5, was placed on two platinum electrodes.

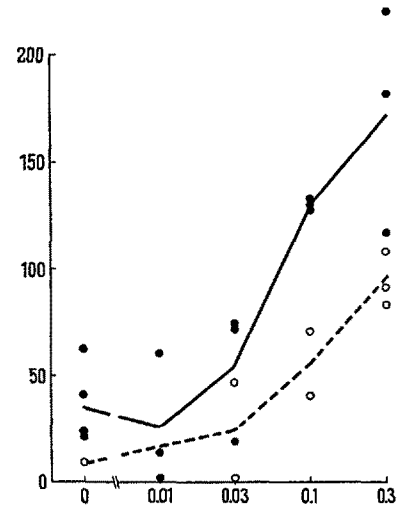
Nerve stimulation (condenser discharges, 20/sec, supramaximal intensity) was applied for 5 sec and maximal change in flow at the initial arterial pressure was measured. Some of the blood flow was then diverted to the jugular vein and another stimulation was effected at the lower perfusion pressure. This procedure was repeated and a series of pressures and corresponding flows were determined, and curves representing the relationship between pressure and flow were plotted. As a measure of the effect of nerve stimulation the change in flow at the perfusion pressure of 80 mm Hg was established by interpolation.

Reserpine (lyophilized reserpine phosphate)[10] was given subcutaneously; all doses refer to the base. In 12 dogs, single doses in the range of 0.01 to 0.3 mg/kg were given 24 h before the experiment; 2 dogs received 10 daily doses of 0.006 mg/kg, the last injection was given 24 h prior to the experiment.

Results. In four normal animals maximal sympathetic stimulation reduced femoral blood flow to 22–63% of the control flow. After a single dose of reserpine, 0.01 mg/kg or 0.03 mg/kg, the response was in the normal range. At 0.1 mg/kg, sympathetic stimulation resulted in an increase rather than a decrease in blood flow, and at 0.3 mg/kg, the increase in flow was very marked (Fig.). In the presence of 1 mg/kg atropine sulfate, increasing doses of reserpine produced graded decreases in the reduction of blood flow so that, after 0.3 mg/kg, maximal sympathetic stimulation altered blood flow only slightly or not at all (see Fig.).

After 10 daily doses of reserpine 0.006 mg/kg (2 preparations), nerve stimulation increased the femoral blood flow to 120% and 170% respectively of the control values. Administration of atropine unmasked a residual constrictor response which reduced blood flow to 60% and 85% respectively of the controls.

Doses of reserpine which are known to reduce the level of norepinephrine in the dog heart[9] also alter the function of the sympathetic fibers innervating the blood vessels of the leg. The single pretreatment dose of 0.1 mg/kg so interferes with vasoconstrictor function in the leg of the dog, that vasoconstriction in response to sympathetic nerve stimulation is overbalanced by vasodilator activity. The same dose of reserpine reduces norepinephrine levels in the heart of the dog to about $^1/_3$ of normal. When this dilator effect, caused by the stimulation of sympathetic cholinergic neurons, is annulled by atropine, a residual vasoconstrictor effect is seen which, however, no longer occurs if the pretreatment dose of reserpine is increased to 0.3 mg/kg. The same dose of reserpine was also required to abolish the effect of sympathetic nerve stimulation on myocardial contractility[9].



Influence of reserpine pretreatment on response of the femoral vascular bed to electrical stimulation of the lumbar sympathetic chain. Sixteen dogs. Pentobarbital anesthesia. Artificial respiration. Heparin 5 mg/kg. Ordinate: blood flow through left femoral artery after stimulation as a percentage of the flow before stimulation of lumbar sympathetic chain at L5, both at a perfusion pressure of 80 mg Hg. Abscissa: dose of reserpine (mg/kg) given 24 h before the experiment. Full circles: without atropine; a solid line joins the means. Open circles: after atropine sulfate 1 mg/kg; a broken line joins the means. For further details see text.

The strong cumulative action of reserpine, emphasized in earlier studies[11,12] is shown by the fact that, in the present experiments, the daily reserpine dose of 0.006 mg/kg given for 10 days is as active as the single dose of 0.1 mg/kg[13].

Zusammenfassung. Die durch sympathische Nervenreizung ausgelöste Vasoconstriktion im Hinterbein des Hundes wird durch Reserpinvorbehandlung aufgehoben. Die dazu benötigten Reserpindosen entsprechen denen, die am Herzen Verlust der Nervenfunktion und des Noradrenalingehaltes hervorrufen.

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Technische Probleme der Hämoglobin-Elektrophorese im Stärkeblock[1]

Die von KUNKEL und WALLENIUS[2] angegebene Stärkeblock-Elektrophorese eignet sich besonders zum Nachweis kleiner Hämoglobin-[3–5] und Myoglobinmengen[6]. Da die im Handel befindlichen Hochspannungs-Elektrophorese-Geräte als Universalapparate ausserordentlich kostspielig sind, haben wir in Zusammenarbeit mit der Firma Therma AG Schwanden (GL Schweiz) einen einfacheren Apparat konstruiert.

Apparatur. Als Kühlelement dient eine 80 × 120 cm messende Kühlplatte Therma aus Metall, wie sie für industrielle und gewerbliche Zwecke serienmässig hergestellt wird. Sie ist mit einer Therma-Kühlmaschine vom Typ LT 2 F 33 mit $^1/_3$ PS Drehstrommotor verbunden und

[1] Die Arbeit wurde mit Hilfe eines Forschungsbeitrages des Schweizerischen Nationalfonds zur Förderung der wissenschaftlichen Forschung durchgeführt.

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